REMARKS

Claims 1-24 are pending, and claims 21-24 have been withdrawn by the Examiner in view of a restriction requirement.

Applicants herein cancel claims 21-24 in view of the imposed restriction requirement and election.

Applicants thank the Examiner for withdrawing the rejections under 35 U.S.C. § 102(a), (b) based on *Chen I*, *Chen II*, *Iacopetta*, and *Hahnel*, and for withdrawing the rejections under 35 U.S.C. § 103(a), in view of *Chen I*, *Chen II*, *Iacopetta*, and *Hahnel*, each in view of *Huang*.

The specification has been objected to in view of applicants' prior amendments to the Sequence Listing. Applicants have herein provided a Declaration with respect to SEQ ID NO:66, and have provided an amended Sequence Listing, and accompanying Statement to obviate this rejection.

Applicants acknowledge the Examiner's new grounds of rejection of particular claims 1-20, under 35 U.S.C. § 112 ¶1, for alleged new matter, and lack of enablement. Applicants have amended the claims to obviate this objection.

Applicants acknowledge the Examiner's rejection of claims 1-3, 5-8, 10 and 20, under 35 U.S.C. § 102(b), as allegedly being anticipated by *Iacopetta*, as defined by *Kyrgidis* et al., J. of Surgical Research, 125:189-212, 2005. Applicants have amended the claims to obviate this rejection.

Applicants acknowledge the Examiner's rejection of claims 15-19, under 35 U.S.C. § 103(a), as being unpatentable over *Iacopetta*, as defined by *Kyrgidis* et al., in view of Huang et al (Human Molecular Genetics, 8:459-470, 1999). Applicants have amended the claims to obviate this rejection.

No new matter has been added.

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FORMALITIES

Priority. The Examiner had previously stated that claims 1-10 and 15-20 are associated with a priority date corresponding to 02 April 2001, whereas claims 11-14 are awarded the benefit of the date of the provisional filing (*i.e.*, 31 March 2000). Applicants contend that in the context of the present amendments, all claims should be awarded the benefit of the date of the provisional filing (*i.e.*, 31 March 2000).

Specification Objection under 35 U.S.C. § 132

Sequence Listing. The Examiner has objected to the prior amendment of the Sequence Listing, under 35 U.S.C. § 132, based on alleged new matter in view of the addition of SEQ ID NOS:66-76.

Specifically, the Examiner states that a Declaration is required to support inclusion of SEQ ID NO: 66 in the Sequence Listing, and that there is insufficient support for inclusion of SEQ ID NO:67, a specific CpG island sequence within SEQ ID NO:66, because the 'cut-off'points (limits) or end positions of SEQ ID NO:67 were not specifically taught. Moreover the Examiner alleges that there is insufficient support for SEQ ID NOS:68-71 (specific treated species of SEQ ID NO:67), because "CpG islands are not necessarily fully up or down methylated, and there is no such teaching in the specification." Finally, the Examiner alleges that there is no support for the MYOD1 amplicon SEQ ID NO:72, or for SEQ ID NOS:73-76 (specific fully up-methylated and fully down-methylated treated species of SEQ ID NO:72) (see Office Action of 10 August 2005, at pages 2-4).

Applicants respectfully disagree with the Examiner on all of these objections, but have nonetheless responsively deleted SEQ ID NOS:67-71 and 73-76 from the presently amended Sequence Listing (attached hereto) to facilitate prosecution.

Applicants, however, respectfully traverse the Examiner's objections with respect to SEQ ID NOS:66 and 72 (now SEQ ID NO:67), based on the fact that in view of applicants' herein provided Declaration, the sequences are fully supported by the originally filed specification.

Specifically, with respect to SEQ ID NO:66, applicants herein provide a Declaration of Peter William Laird (attached hereto), declaring that the MYOD sequence presently submitted as SEQ ID NO:66 is the same as the MYOD sequence as it existed in GenBank at the time the invention was made, prior to the filing of the instant application or of the underlying provisional application. This conclusion is not only supported by Dr. Laird's own records and analysis, but is also confirmed by the fact that the last update to the AF027148 sequence was on 07 AUG 1998 (see APPENDIX B of the Declaration, which is the current GenBank record for this sequence). Therefore, SEQ ID NO:66 is fully supported.

Additionally, with respect to SEQ ID NO:72 (now SEQ ID NO:67), the specification (at page 30, Table II, 5th column from left in the MYOD1 row), explicitly teaches the amplicon of SEQ ID NO:72 (now SEQ ID NO:67) by providing the amplicon end-points within the MYOD1 gene (i.e., within SEQ ID NO:66). Therefore, SEQ ID NO: 72 (now SEQ ID NO:67) represents an amplified portion (amplicon) of SEQ ID NO:66.

Applicants thus respectively request that this objection be withdrawn.

Rejections under 35 U.S.C. § 112 ¶1

New matter

Claims 1-20 were rejected by the Examiner, under 35 U.S.C. § 112 ¶1, for alleged new matter.

Specifically, the Examiner asserts that applicants' recitation of "an esophageal cancer related condition" and "at least one" genomic CpG sequence introduce new matter. The Examiner states that while the specification provides support for Barrett's esophagous, Barrett's intestinal tissue, esophageal dysplasia and esophageal metaplasia, there is insufficient support in the specification for recitation of a genus of "an esophageal cancer related condition" (Office Action of 10 August 2006, at page 8).

Applicants have amended independent claim 1 to recite "Barrett's esophagous, Barrett's intestinal tissue, esophageal adenocarcinoma, esophageal dysplasia, esophageal metaplasia, pre-

cancerous conditions in normal esophageal squamous mucosa, and combinations thereof," in place of "an esophageal cancer related condition," thereby obviating this aspect of the Examiner's rejection. Support for this amendment is found throughout the originally filed specification, and in particular, for example, in original claim 13 and the working Examples.

Applicants respectfully traverse the Examiner's assertion that there is insufficient support for recitation of "at least one." Such recitation is supported in the specification, for example, at page 8, under Definition of "methylation state" and "hypermethylation" (wherein "at least one" is explicitly recited), at page 14, lines 27 or 32, page 15, lines 5-6, page 1, and line 28 (reciting the inventive determination of "methylation state," which is defined to include "at least one."

Applicants, therefore, respectfully request withdrawal of the Examiner's rejection of claims 1-20, under 35 U.S.C. § 112 ¶1, in view of applicants above described claim amendments.

Enablement

Claims 1-20 were also rejected by the Examiner, under 35 U.S.C. § 112 ¶1, for alleged lack of enablement.

Specifically, the Examiner alleges that "the specification, while being enabling for a method of diagnosing or prognosing of esophageal cancer, esophageal dysplasia, esophageal metaplasia, or Barrett's intestinal tissue, in an esophageal tissue sample by detecting hypermethylation of CpG islands in the MYOD1 gene as compared to normal esophageal tissue" does not reasonably provide enablement for diagnosis or prognosis of any esophageal cancer related condition by detecting any type of methylation such as hypermehthylation, hypomethylation or normal methylation in at least one CpG sequence in the MYOD1 gene" (Office Action of 10 August 2006, at page 9).

Applicants have responsively amended *independent* claim 1 to obviate this rejection. In addition to the above described claim 1 amendment, applicants have amended independent claim 1 to recite "hypermethylation." Support for this amendment is found throughout the originally filed specification, and in particular, for example, in original claim 20 and the working Examples. *Dependent* claim 20 has been cancelled herein, in view of this amendment to *independent* claim 1.

Applicants, therefore, respectfully request withdrawal of the Examiner's rejection of claims 1-20, under 35 U.S.C. § 112 ¶1, in view of applicants above described claim amendments.

Rejections under 35 U.S.C. § 102

Iacopetta. Claims 1-3, 5-8, 10 and 20 have been rejected by the Examiner, under 35 U.S.C. § 102(b), as allegedly being anticipated by *Iacopetta*, as defined by *Kyrgidis* et al., J. of Surgical Research, 125:189-212, 2005.

Specifically, applicants prior recitation of "esophageal cancer related condition," has been interpreted by the Examiner to encompass colorectal cancer (as taught by *Kyrgidi*), and the Examiner further alleges that Iacopetta teaches regional hypermethylation of a 3' downstream region of MYOD1 in relation to colorectal neoplasia, and thus teaches diagnosis or prognosis thereof. The Examiner further states that the present claims have been "interpreted to encompass the gene that can be analyzed by the recited SEQ ID NOS in the claim." but that they "do not require analysis with the specifically recited SEQ ID NOS" (Office Action of 10 August 2006, at pages 16-17).

Applicants, as described above, have amended the claims to obviate this rejection by deleted the prior recitation of "esophageal cancer related condition."

Applicants, therefore, respectfully request withdrawal of this 35 U.S.C. § 102(b)-based rejection of claims 1-3, 5-8, 10 and 20, based on applicants' above described amendments to *independent* claim 1.

Rejections under 35 U.S.C. § 103

Iacopetta, as defined by Kyrgidis, in view of Huang. Claims 15-19 have been rejected, under 35 U.S.C. § 103(a), as being unpatentable over *Iacopetta*, as defined by *Kyrgidis* et al., in view of Huang et al (Human Molecular Genetics, 8:459-470, 1999).

Specifically, the Examiner asserts that Iacopetta teaches that regional hypermehthylation of the 3' downstream region of MYOD1 is an early and widespread event in colorectal neoplasias, and that such hypermethylation is strongly associated with the development of benign and malignant

colorectal tumors. The Examiner further states that while Iacopetta does not teach DMH methylation analysis, Huang nonetheless does teach the use of DMH array-based methods, and that it would have been *prima facie* obvious to one of ordinary skill at the time of the invention was make to improve the analysis method used by Iacopetta, with the more precise DHM analysis of Huang, and with a reasonable expectation of success.

Applicants, as described above, have amended the claims to obviate this rejection by deleted the prior recitation of "esophageal cancer related condition."

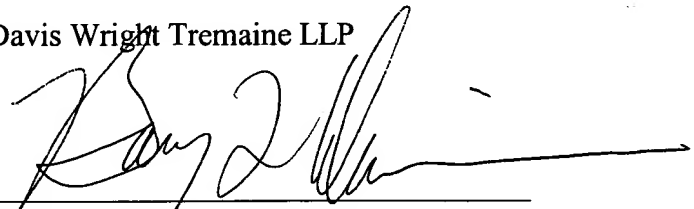
Applicants, therefore, respectfully request withdrawal of this 35 U.S.C. § 103(a)-based rejection of claims 1-3, 5-8, 10 and 20, based on applicants' above described amendments to *independent* claim 1.

CONCLUSION

In view of the foregoing amendments and remarks, applicants respectfully request entry of the present Response and Amendment, and allowance of all pending claims. The Examiner is encouraged to phone applicants' attorney, Barry L. Davison, to resolve any outstanding issues and expedite allowance of this application.

Respectfully submitted,

Davis Wright Tremaine LLP



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